

# Pre and postoperative evaluation of transcranial Doppler pulsatility index of the middle cerebral artery in patients with severe carotid artery stenosis



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**Pre and postoperative evaluation of transcranial Doppler pulsatility index of the middle cerebral artery in patients with severe carotid artery stenosis**

*In the management of severe carotid artery stenosis particular importance must be given to the evaluation of the risk of perioperative cerebral ischemic events. Our study analysed the possible relationship between the pre-operative middle cerebral artery Gosling Index, calculated after transcranial Doppler (TCD), and intra-operative stump pressure (SP), in order to identify patients with higher risk of ischemic accidents. Moreover, we studied pre- and post-operative Gosling Index values in association with possible events during follow-up. In a one-year time lapse 47 patients underwent either carotid endarterectomy (CEA) or carotid artery stenting (CAS) with proximal embolic protection system. All patients were subject to pre- and post-operative TCD with calculation of the Gosling Index and intra-operative SP. We observed that higher pre-operative Gosling Index values are associated with lower intra-operative SP values, elements that represent a higher risk for cerebro-vascular ischemic accidents; this result is particularly evident when observing the diabetic sub-population. An increase in ischemic events did not present statistically significant differences when observing the populations treated with CEA or CAS. TCD and SP are valid and simple exams that can help identify precociously patients with a higher risk of cerebro-vascular accidents related to surgical or endovascular treatment.*

KEY WORDS: Carotid artery stenosis, Carotid endarterectomy, Endovascular treatment

## Introduction

Carotid artery stenosis is the second cause for brain stroke, therefore a relatively frequent and potentially highly invalidating and lethal pathology<sup>1,2</sup>. When man-

aging severe carotid artery stenosis, with the aim of preventing or limiting the incidence of cerebral stroke, the therapeutic choices stand between carotid endarterectomy (CEA) or carotid artery stenting (CAS), along with the control of risk factors and the best medical therapy<sup>3,4</sup>. The use of transcranial Doppler before, during and after carotid endarterectomy is a well-known and well-established technique for the evaluation of cerebral hemodynamic<sup>5,6</sup>. In order to evaluate the risk of cerebral ischemic events during carotid artery cross-clamping, we studied the correlation between the middle cerebral artery Gosling Index, calculated during transcranial Doppler (TCD), and the intra-operative stump pressure (SP). The pre- and post-operative values of Gosling Index were also associated with the clinical outcomes.

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## Materials and Methods

Between April 2014 and April 2015, 50 patients (40 males and 10 females) affected by hemodynamic carotid artery stenosis were observed at our Centre. All patients underwent pre- and post-operative TCD monitoring (EZ-dop, DWL, Compumedics Germany GmbH) with a 2 MHz probe placed at the thinnest point of the temporal bone. The pulsatility index (Gosling Index) of the middle cerebral artery of the ipsilateral carotid stenosis, was calculated using a formula based on the measurement of pre-operative TCD values (peak systolic velocity, end diastolic velocity and mean velocity during a cardiac cycle). For all patients the past medical history was remarkable for hypertension, other relevant risk factors were: smoking (68%), dislipidemia (84%), chronic renal failure (24%), diabetes mellitus (64%) and ischemic heart disease (72%). The carotid artery stenosis were evaluated using Duplex-scan with the European Carotid Surgery Trial (ECST) method. Furthermore all patients underwent a higher level imaging examination with contrast-enhanced Computerized Tomography (Angio-CT) or Magnetic Resonance Imaging (MRI) beside basal brain CT-scan <sup>7</sup>. During the period of observation other 25 patients were treated with CEA or CAS but could not be included in the study: 17 underwent CAS with distal embolic protection device and 8 were not subject to TCD.

In order to be enrolled patients needed had to present the eligibility criteria for carotid artery revascularization according to the American Heart Association (AHA): carotid artery stenosis evaluated in non-invasive imaging as >70% or >50% for catheter angiography in subjects asymptomatic for brain ischemic events or symptomatic within the previous six months <sup>8</sup>.

The choice between CEA or CAS was done based on clinical symptoms, patient's age, risk factors and the plaque's morphological characteristics, along with the degree of stenosis and the eventuality of a contralateral carotid steno-occlusion. The sonographic characterization of the plaque was done according to the Gray-Weale (GW) classification <sup>9</sup>: 1<sup>st</sup> degree-homogeneous hypochoic plaque; 2<sup>nd</sup> degree- mainly hypochoic plaque; 3<sup>rd</sup> degree-mainly hyperechoic plaque; 4<sup>th</sup> degree- homogeneous hyperechoic plaque; 5<sup>th</sup> degree- fibrous-calcific plaque with acoustic shadow.

All CEA were performed under general anaesthesia. After longitudinal incision along the anterior margin of the sternocleidomastoid muscle, the common, external and internal carotid arteries were exposed, with respect for the cranial nerves. For all patients the classic carotid repair was preferred, followed by direct suture or the application of a patch. Patients who underwent CAS were treated using the Mo.Ma (Medtronic, Santa Rosa, California, USA) proximal occluding embolic protection system, during which the SP could be measured. The procedure was carried out under local anaesthesia and through a 9 Fr transfemoral access. After aortography of

the arch, the external carotid artery (ECA) and later its distal branches, as the temporal superficial or the occipital artery, were catheterized. After positioning an extra-stiff guide wire, the Mo.Ma device was introduced, with the blowing of two balloons, one at the origin of the ECA and one in the common carotid artery (CCA), in order to block the blood flow. With its double lumen inside it is possible to pass the stenotic lesion with a coronary guide wire, release the stent and thereafter, dilate it without provoking the embolic debris <sup>10</sup>.

Statistical Analysis: In order to compare continuous variables the "U" test of Mann-Whitney was used, while categorical variables (gender, risk factors,...) required the use of the Chi-Squared test or the Fisher's exact test. Only values of  $p < 0.05$  were considered statistically significant.

## Results

Of the 50 patients included in the study, during carotid Duplex-scan the plaques observed were: GW1= 8%, GW2= 48%, GW3= 28%, GW4= 16% and GW5= 0%. Before treatment two patients presented the occlusion of the contralateral carotid artery. It was possible to study the middle cerebral artery in 47 patients, at a depth of about 50 mm. In the remaining three patients the acoustic window was inadequate for a valid evaluation. The parameters recorded during the Duplex-scan examination were: the peak systolic velocity (PSV), the average velocity in the middle cerebral artery (MCAV) and the Gosling Index in the middle cerebral artery. All the TCD values were registered and calculated the day before surgery and 30 days after the operation. Of the 47 patients in which it was possible to perform the TCD, 24 (51%) were symptomatic for cerebral ischemic events in the six months preceding the surgery and presented an average PSV after the stenosis of  $302 \pm 45$  cm/s, a Gosling Index of  $0.89 \pm 0.23$  and an average MCAV of  $55.1 \pm 13$  cm/s. The remaining 23 patients were asymptomatic and presented an average PSV of  $387 \pm 34$  cm/s, Gosling Index of  $1.22 \pm 0.15$  and an average MCAV of  $58.3 \pm 16$  cm/s. The data presents a statistically significant difference of the Gosling Index between the two groups of patients ( $p = 0.072$ ), but no statistically significant differences for the remaining parameters.

The treatment chosen was for 36 patients (76.6%) the CEA and for 11 (23.4%) the CAS with Mo.Ma (Medtronic, Santa Rosa, California, USA) proximal embolic protection system. In all cases an intra-operative stump pressure (SP) was measured and the average value resulted to be  $63 \pm 22$  mmHg. There has been a statistically significant difference between the two groups when observing the intra-operative SP values: the CEA group had average  $53 \pm 16$  mmHg while the CAS had average  $59 \pm 20$  mmHg ( $p < 0.001$ ). Two patients treated with open surgery required the use of a shunt for

TABLE I - Pre-operative Gosling Index: symptomatic vs asymptomatic patients.

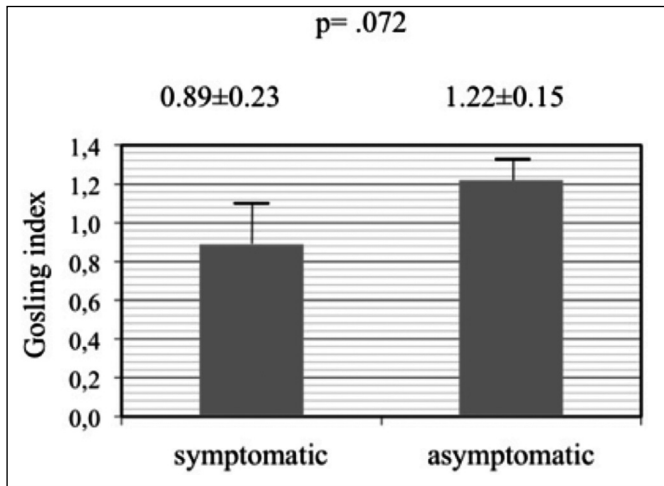


TABLE II - Pre-operative Gosling Index: diabetic vs non-diabetic patients.

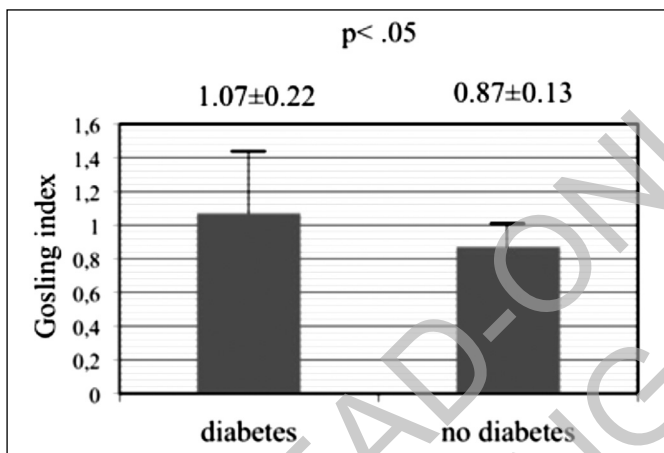
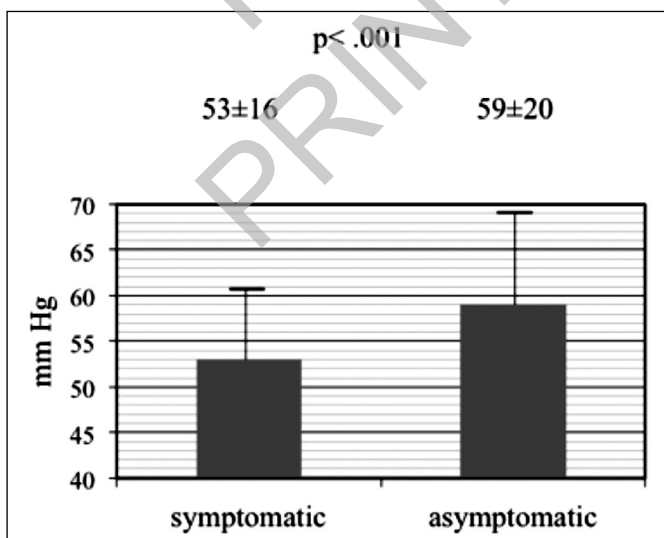


TABLE III - Intra-operative Stump Pressure: symptomatic vs asymptomatic patients.



the drop of SP <35 mmHg; both were diabetic with poor control of the blood glucose level and presented higher values of the Gosling Index. No significant correlation was found when evaluating the pre-operative Gosling Index and the need for shunting during surgery (p= 0.682). In all groups observed, no patients deceased or presented either cerebral infarction or stroke in the peri-operative period. During follow-up two asymptomatic carotid artery occlusions occurred in patients who had underwent CEA. After 30 days from treatment the following results were recorded: average MCAV 43.61 ± 22 cm/s, average Gosling Index 1.14 ± 0.21. The data did not present statistically significant differences between the two groups (p >0.05). Other results are shown in Table I, II and III.

## Discussion

When dealing with symptomatic or asymptomatic high level carotid artery stenosis the possible therapeutic procedures are either CEA or CAS with embolic protection devices (proximal or distal) <sup>11,12</sup>. CEA nowadays is the gold standard for the extracranial carotid revascularization, especially in symptomatic patients with stenosis of 70% or higher. Recent meta-analysis have demonstrated a risk of restenosis greater than 50% in 10% of patients after 2 years from carotid surgery <sup>12,13</sup>. Since a few years, CAS has emerged as a potentially valid alternative to CEA, because it permits to avoid a general or broad local anaesthesia and a surgical incision, bringing a higher compliance from the patients along with a lower number of peri-procedural cardiac complications, lower cranial nerve injuries and a shorter hospitalization.

Calculating Gosling Index helps to evaluate any possible reduction of the brain's haematic reservoir <sup>14</sup>, in order to identify preventively which patients could undergo cerebral haemorrhage or stroke for hyper-perfusion syndrome after CEA <sup>6,14</sup>. In our study we tried to identify before surgery the risk of brain ischemia secondary to carotid cross-clamping through the use of Gosling Index and TCD. Post-operative parameters 30 days after surgery were compared to the possible appearance of symptoms. Although none of the patients presented ischemic lesions at the arterial clamping and/or post-operative stroke, Gosling Index has resulted inversely related to the intra-operative stump pressure (SP). Moreover, patients with SP ≤ 35 mmHg had a Gosling Index significantly higher when compared to patients with SP ≥ 35 mmHg. A particular attention was paid to the diabetic subpopulation: overall patients affected by diabetes presented lower SP and higher Gosling Index values.

In the past 30 years SP had proven to be a valid test during carotid artery surgery and it is also simple and cheap. With the goal of reducing as much as possible the risk of intra-operative stroke, many Authors have

introduced various alternative methods to the SP to identify precociously and prevent arterial clamping ischemia: electroencephalogram (EEG), TCD, evoked potentials and cerebral transcutaneous oxymetry are all widely described diagnostic methods for brain ischemia, but none of them has been proved to be better than the SP measurement<sup>6</sup>. Up to date no pre-operative instrumental imaging technique is 100% correlated to the need of an intra-operative shunt. A highly valid method to identify intra-operative ischemia is the use of loco-regional anesthesia, which allows to check constantly the brain functions through beep-test and direct communication with the patient. The GALA Trial did not demonstrate the loco-regional anaesthesia to be better than the general anaesthesia during CEA; the only situation in which a less extended anaesthesia has proven to be a better choice is when treating patients presenting a contralateral carotid occlusion, however such result was not statistically significant<sup>15</sup>.

The study we conducted was prospective, during which two cohorts of patients were observed: one treated with open surgery (CEA) and one by endovascular technique (CAS). One of the major limits of the study was the small number of patients enrolled along with the discrepancy between endarterectomies versus stentings. Stump pressure levels resulted significantly higher for patients who underwent CAS with Mo.Ma proximal cerebral protection device; such result could have been affected by several overestimating factors: first of all CAS are conducted under local anaesthesia which implies working with the patient awake, situation exposed to higher blood pressure and therefore SP levels; second, the Mo.Ma system is effective when both the common and external carotid arteries are occluded, however anomalies of the superior thyroid artery (low emergency level, incomplete clamping, etc), first branch of the external carotid artery, can provoke retrograde blood flow with increase in SP values.

## Conclusions

The conclusions that can be drawn from our study are that: when comparing CEA and CAS, higher post-operative Gosling Index values are associated with lower intra-operative SP measurements, which represents a higher risk of cerebro-vascular ischemic complications. Although there is no significant difference between the two groups of treatment, the relationship is particularly evident when observing the diabetic subpopulation. TCD with the following calculation of the Gosling Index, is a cheap, easily conducted and non-invasive exam that allows a valid study of intra-cerebral haemodynamics. The same observations can be done for the invasive measurement of SP, which proved to be a highly sensible exam optimal for intra-operative evaluations.

## Riassunto

Il Doppler transcranico (TCD) viene frequentemente utilizzato per la valutazione delle resistenze periferiche cerebrali e del flusso cerebrale a livello dell'arteria cerebrale media sia prima che durante chirurgia carotidea. Nella gestione della stenosi carotidea severa particolare importanza deve essere data alla valutazione del rischio di eventi ischemici cerebrali intraoperatori. Il nostro studio ha analizzato la possibile relazione tra l'indice di Gosling dell'arteria cerebrale media, calcolato mediante TCD pre-operatorio e la Stump Pressure (SP) intra-operatoria, al fine di identificare i pazienti con elevato rischio di eventi ischemici. Inoltre, abbiamo registrato l'indice di Gosling pre e post operatorio correlandolo con possibili eventi durante il follow-up. In un lasso di tempo di un anno 47 pazienti sono stati sottoposti ad endoarteriectomia carotidea (CEA) o stenting carotideo (CAS) con sistema di protezione embolica prossimale. Tutti i pazienti sono stati sottoposti a TCD pre e post-operatorio con calcolo dell'Indice Gosling e SP intra-operatoria. Abbiamo osservato che l'aumento di valori pre-operatori dell'Indice di Gosling sono associati a più bassi valori intra-operatori di SP, elementi che rappresentano un rischio più elevato di incidenti ischemici cerebrovascolari; Questo risultato è particolarmente evidente quando si osserva la sotto-popolazione di pazienti diabetici. Non vi è stata alcuna differenza statisticamente significativa, per quanto concerne eventi ischemici perioperatori, tra i pazienti sottoposti a CEA o CAS. Il TCD e la SP sono esami validi e semplici che possono aiutare a identificare precocemente i pazienti con un rischio più elevato di incidenti cerebro-vascolari correlati al trattamento chirurgico o endovascolare.

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